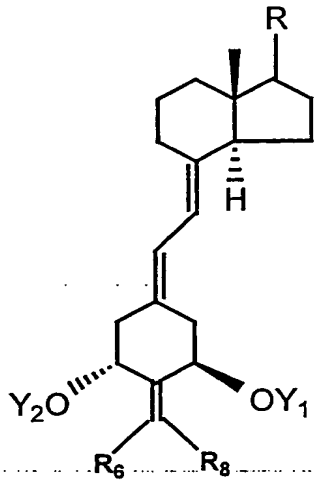
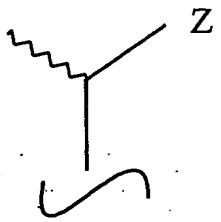
CLAIMS

We claim:

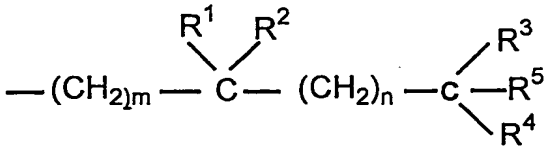
1. A compound having the formula:



where Y_1 and Y_2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R_6 and R_8, which may be the same or different, are each selected from hydrogen, alkyl, hydroxyalkyl and fluoroalkyl, or, when taken together represent the group $-(CH_2)_x-$ where x is an integer from 2 to 5, and where the group R is represented by the structure:

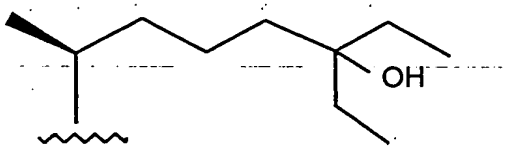


where the stereochemical center at carbon 20 may have the R or S configuration, and where Z is selected from Y, -OY, $-CH_2OY$, -C CY and -CH=CHY, and $-CH_2CH_2CH=CR^3R^4$, where the double bond may have the cis or trans geometry, and where Y is selected from hydrogen, methyl, $-COR^5$ and a radical of the structure:

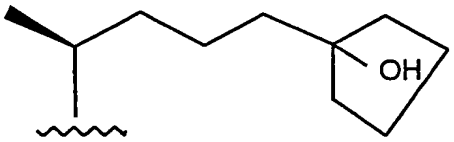


where m and n, independently, represent the integers from 0 to 5, where R^1 is selected from hydrogen, deuterium, hydroxy, protected hydroxy, fluoro, trifluoromethyl, and C_{1-5}-alkyl, which may be straight chain or branched and, optionally, bear a hydroxy or protected-hydroxy substituent, and where each of R^2, R^3, and R^4, independently, is selected from deuterium, deuteroalkyl, hydrogen, fluoro, trifluoromethyl and C_{1-5} alkyl, which may be straight-chain or branched, and optionally, bear a hydroxy or protected-hydroxy substituent, and where R^1 and R^2, taken together, represent an oxo group, or an alkylidene group, $=CR^2R^3$, or the group $-(CH_2)_p-$, where p is an integer from 2 to 5, and where R^3 and R^4, taken together, represent an oxo group, or the group $-(CH_2)_q-$, where q is an integer from 2 to 5, and where R^5 represents hydrogen, hydroxy, protected hydroxy, C_{1-5} alkyl or $-OR^7$ where R^7 represents C_{1-5} alkyl, and wherein any of the CH-groups at positions 20, 22, or 23 in the side chain may be replaced by a nitrogen atom, or where any of the groups $-CH(CH_3)-$, $-CH(R^3)-$, or $-CH(R^2)-$ at positions 20, 22, and 23, respectively, may be replaced by an oxygen or sulfur atom.

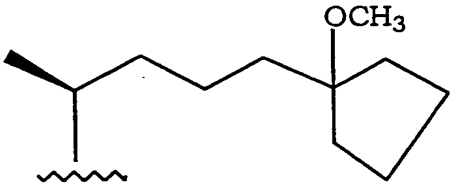
2. The compound of claim 1 where R is a side chain of the formula



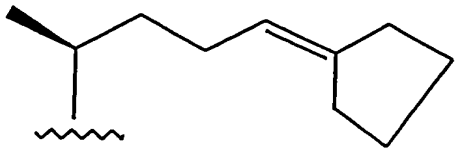
3. The compound of claim 1 where R is a side chain of the formula



4. The compound of claim 1 where R is a side chain of the formula



5. The compound of claim 1 where R is a side chain of the formula



6. 20(S)-1α,25-dihydroxy-2-methylene-26,27-dihomo-19-norvitamin D_3.

7. 20(S)-26,27-dimethylene-25-methoxy-2-methylene-19-norvitamin D_3.

8. 20(S)-1α,25-dihydroxy-26,27-dimethylene-2-methylene-19-norvitamin D_3.

9. 20(S)-26,27-dimethylene-1α-hydroxy-2-methylene-24-dehydro-19-norvitamin D_3.

10. A pharmaceutical composition containing at least one compound as claimed in claim 1 together with a pharmaceutically acceptable excipient.

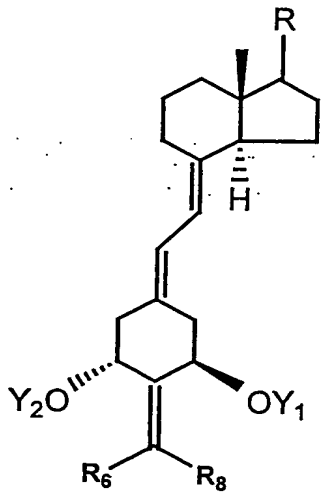
11. The pharmaceutical composition of claim 10 containing 20(S)-1α,25-dihydroxy-2-methylene-26,27-dihomo-19-norvitamin D_3 in an amount from about 0.1μg to about 50μg.

12. The pharmaceutical composition of claim 10 containing 20(S)-26,27-dimethylene-25-methoxy-2-methylene-19-norvitamin D_3 in an amount from about 0.1μg to about 50μg.

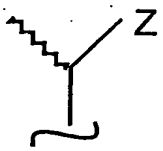
13. The pharmaceutical composition of claim 10 containing 20(S)-1α,25-dihydroxy-26,27-dimethylene-2-methylene-19-norvitamin D_3 in an amount of from about 0.1μg to about 50μg.

14. The pharmaceutical composition of claim 10 containing 20(S)-26,27-dimethylene-1α-hydroxy-2-methylene-24-dehydro-19-norvitamin D_3 in an amount from about 0.1μg to about 50μg.

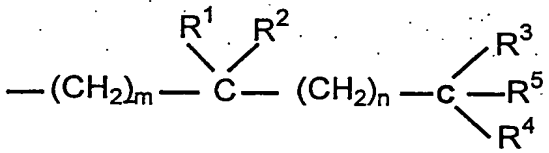
15. A method of treating metabolic bone disease where it is desired to maintain or increase bone mass comprising administering to a patient with said disease an effective amount of a compound having the formula:



where Y_1 and Y_2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R_6 and R_8, which may be the same or different, are each selected from hydrogen, alkyl, hydroxyalkyl and fluoroalkyl, or, when taken together represent the group $-(CH_2)_x-$ where x is an integer from 2 to 5, and where the group R is represented by the structure:



where the stereochemical center at carbon 20 may have the R or S configuration, and where Z is selected from Y, -OY, $-CH_2OY$, -C≡CY, -CH=CHY, and $-CH_2CH_2CH=CR^3R^4$, where the double bond may have the cis or trans geometry, and where Y is selected from hydrogen, methyl, $-COR^5$ and a radical of the structure:



where m and n, independently, represent the integers from 0 to 5, where R^1 is selected from hydrogen, deuterium, hydroxy, protected hydroxy, fluoro, trifluoromethyl, and C_{1-5}-alkyl, which may be straight chain or branched and, optionally, bear a hydroxy or protected-hydroxy substituent, and where each of R^2, R^3, and R^4, independently, is selected from deuterium, deuteroalkyl, hydrogen, fluoro, trifluoromethyl and C_{1-5} alkyl, which may be straight-chain

or branched, and optionally, bear a hydroxy or protected-hydroxy substituent, and where R^1 and R^2, taken together, represent an oxo group, or an alkylidene group, $=CR^2R^3$, or the group $-(CH_2)_p-$, where p is an integer from 2 to 5, and where R^3 and R^4, taken together, represent an oxo group, or the group $-(CH_2)_q-$, where q is an integer from 2 to 5, and where R^5 represents hydrogen, hydroxy, protected hydroxy, C_{1-5} alkyl or $-OR^7$ where R^7 represents C_{1-5} alkyl, and wherein any of the CH-groups at positions 20, 22, or 23 in the side chain may be replaced by a nitrogen atom, or where any of the groups $-CH(CH_3)-$, $-CH(R^3)-$, or $-CH(R^2)-$ at positions 20, 22, and 23, respectively, may be replaced by an oxygen or sulfur atom.

16. The method of claim 15 where the disease is senile osteoporosis.

17. The method of claim 15 where the disease is postmenopausal osteoporosis.

18. The method of claim 15 where the disease is steroid-induced osteoporosis.

19. The method of claim 15 where the disease is low bone turnover osteoporosis.

20. The method of claim 15 where the disease is osteomalacia.

21. The method of claim 15 where the disease is renal osteodystrophy.

22. The method of claim 15 wherein the compound is administered orally.

23. The method of claim 15 wherein the compound is administered parenterally.

24. The method of claim 15 wherein the compound is administered transdermally.

25. The method of claim 15 wherein the compound is administered in a dosage of from 0.1μg to 50μg per day.

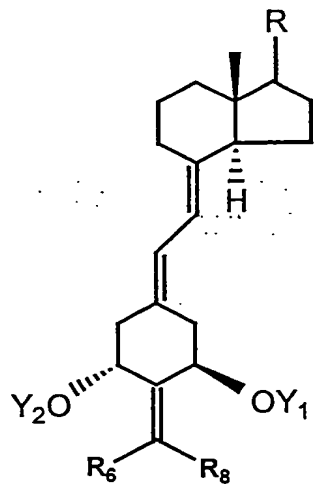
26. The method of claim 15 wherein the compound is 20(S)-1α,25-dihydroxy-2-methylene-26,27-dihomo-19-norvitamin D_3.

27. The method of claim 15 wherein the compound is 20(S)-26,27-dimethylene-25-methoxy-2-methylene-19-norvitamin D_3.

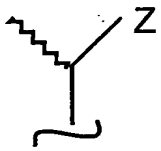
28. The method claim 15 wherein the compound is 20(S)-1α,25-dihydroxy-26,27-dimethylene-2-methylene-19-norvitamin D_3.

29. The method of claim 15 wherein the compound is 20(S)-26,27-dimethylene-1α-hydroxy-2-methylene-24-dehydro-19-norvitamin D_3.

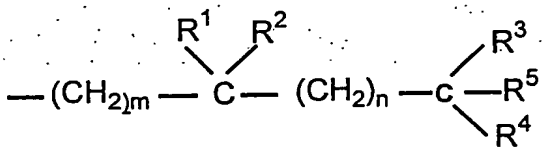
30. A method of treating psoriasis comprising administering to a patient with said disease an effective amount of a compound having the formula:



where Y_1 and Y_2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R_6 and R_8, which may be the same or different, are each selected from hydrogen, alkyl, hydroxyalkyl and fluoroalkyl, or, when taken together represent the group $-(CH_2)_x-$ where x is an integer from 2 to 5, and where the group R is represented by the structure:



where the stereochemical center at carbon 20 may have the R or S configuration, and where Z is selected from Y, -OY, $-CH_2OY$, -C≡CY, -CH=CHY, and $-CH_2CH_2CH=CR^3R^4$, where the double bond may have the cis or trans geometry, and where Y is selected from hydrogen, methyl, $-COR^5$ and a radical of the structure:



where m and n, independently, represent the integers from 0 to 5, where R^1 is selected from hydrogen, deuterium, hydroxy, protected hydroxy, fluoro, trifluoromethyl, and C_{1-5}-alkyl, which may be straight chain or branched and, optionally, bear a hydroxy or protected-hydroxy substituent, and where each of R^2, R^3, and R^4, independently, is selected from deuterium, deuteroalkyl, hydrogen, fluoro, trifluoromethyl and C_{1-5} alkyl, which may be straight-chain

or branched, and optionally, bear a hydroxy or protected-hydroxy substituent, and where R^1 and R^2, taken together, represent an oxo group, or an alkylidene group, $=CR^2R^3$, or the group $-(CH_2)_p-$, where p is an integer from 2 to 5, and where R^3 and R^4, taken together, represent an oxo group, or the group $-(CH_2)_q-$, where q is an integer from 2 to 5, and where R^5 represents hydrogen, hydroxy, protected hydroxy, C_{1-5} alkyl or $-OR^7$ where R^7 represents C_{1-5} alkyl, and wherein any of the CH-groups at positions 20, 22, or 23 in the side chain may be replaced by a nitrogen atom, or where any of the groups $-CH(CH_3)-$, $-CH(R^3)-$, or $-CH(R^2)-$ at positions 20, 22, and 23, respectively, may be replaced by an oxygen or sulfur atom.

31. The method of claim 30 wherein the compound is 20(S)-1α,25-dihydroxy-2-methylene-26,27-dihomo-19-norvitamin D_3.

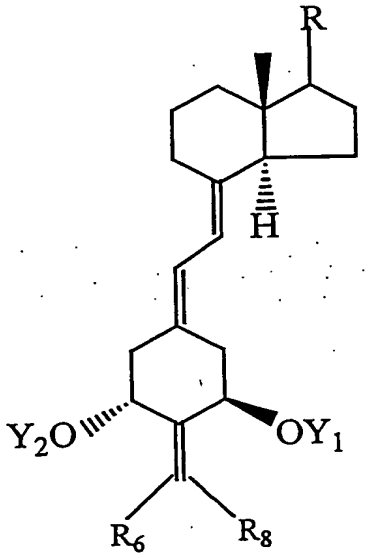
32. The method of claim 30 wherein the compound 20(S)-26,27-dimethylene-25-methoxy-2-methylene-19-norvitamin D_3.

33. The method of claim 30 wherein the compound is 20(S)-1α,25-dihydroxy-26,27-dimethylene-2-methylene-19-norvitamin D_3.

34. The method of claim 30 wherein the compound is 20(S)-26,27-dimethylene-1α-hydroxy-2-methylene-24-dehydro-19-norvitamin D_3.

35. The method of claim 30 wherein said effective amount comprises about 0.01μg/day to about 100μg/day of said compound.

36. A method of treating a cancerous disease comprising administering to a patient with said disease an effective amount of a compound having the formula:



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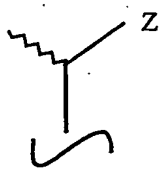
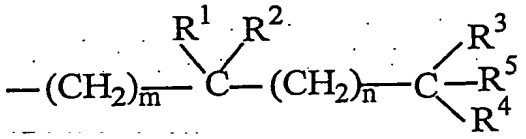
where Y_1 and Y_2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R_6 and R_8, which may be the same or different, are selected from hydrogen, alkyl, hydroxyalkyl and fluoroalkyl, or, when taken together represent the group $-(CH_2)_x-$ where x is an integeer from 2 to 5, and where the group R is represented by the structure:



where the stereochemical center at carbon 20 may have the R or S configuration, and where Z is selected from Y, -OY, $-CH_2OY$, -C≡CY, -CH=CHY, and $-CH_2CH_2CH=CR^3R^4$, where the double bond may have the cis or trans geometry, and where Y is selected from hydrogen, methyl, $-COR^5$ and a radical of the structure:



where m and n, independently, represent the integers from 0 to 5, where R^1 is selected from hydrogen, deuterium, hydroxy, protected hydroxy, fluoro, trifluoromethyl, and C_{1-5}-alkyl, which may be straight chain or branched and, optionally, bear a hydroxy or protected-hydroxy substituent, and where each of R^2, R^3, and R^4, independently, is selected from deuterium, deuteroalkyl, hydrogen, fluoro, trifluoromethyl and C_{1-5} alkyl, which may be straight-chain or branched, and optionally, bear a hydroxy or protected-hydroxy substituent, and where R^1 and R^2, taken together, represent an oxo group, or an alkylidene group, $=CR^2R^3$, or the group $-(CH_2)_p-$, where p is an integer from 2 to 5, and where R^3 and R^4, taken together, represent an oxo group, or the group $-(CH_2)_q-$, where q is an integer from 2 to 5, and where R^5 represents hydrogen, hydroxy, protected hydroxy, C_{1-5} alkyl or $-OR^7$ where R^7 represents C_{1-5} alkyl, and wherein any of the CH-groups at positions 20, 22, or 23 in the side chain may be replaced by a nitrogen atom, or where any of the groups $-CH(CH_3)-$, $-CH(R^3)-$, or $-CH(R^2)-$ at positions 20, 22, and 23, respectively, may be replaced by an oxygen or sulfur atom.

37. The method of claim 36 where the disease is leukemia.

38. The method of claim 36 where the disease is colon cancer.

39. The method of claim 36 where the disease is breast cancer.

40. The method of claim 36 where the disease is prostate cancer.

41. The method of claim 36 wherein the compound is administered orally.

42. The method of claim 36 wherein the compound is administered parenterally.

43. The method of claim 36 wherein the compound is administered transdermally.

44. The method of claim 36 wherein the compound is 20(S)-1α,25-dihydroxy-2-methylene-26,27-dihomo-19-norvitamin D_3.

45. The method of claim 36 wherein the compound is 20(S)-26,27-dimethylene-25-methoxy-2-methylene-19-norvitamin D_3.

46. The method of claim 36 wherein the compound is 20(S)-1α,25-dihydroxy-26,27-dimethylene-2-methylene-19-norvitamin D_3.

47. The method of claim 36 wherein the compound is 20(S)-26,27-dimethylene-1α-hydroxy-2-methylene-24-dehydro-19-norvitamin D_3.

48. The method of claim 36 wherein the compound is administered in a dosage of from 0.1μg to 50μg per day.